A 57-year-old white woman who had never smoked presented with a history of isolated coughing for several months. Computed tomography scans of the chest demonstrated a 2.5 × 4.5-cm right-middle-lobe tumor, widespread bilateral pulmonary nodules consistent with metastases, and enlarged lymph nodes in the subcarinal, paratracheal, and prevascular regions (Fig 1, yellow arrows). Fine-needle aspiration biopsy of the lesion revealed bronchogenic adenocarcinoma. Magnetic resonance imaging of the brain revealed four subcentimeter metastatic lesions with minimal edema. Polymerase chain reaction-based sequencing of DNA of the epidermal growth factor receptor (EGFR) gene revealed an 18-base pair deletion in exon 19 of the EGFR gene, which has been previously reported in patients with lung tumors that responded to erlotinib.1,2 The patient received whole-brain radiation therapy with a total of 30 Gy in ten fractions. She then received systemic front-line therapy with single agent erlotinib (standard oral dose, 150 mg). Her disease demonstrated a major response to erlotinib; the diffuse pulmonary nodules disappeared 6 weeks after she started therapy, while the primary right-middle–lobe tumor shrank down to 1.0 cm2 2 months later and remained stable for over 1 year (Fig 1). Thirteen months after the initiation of systemic therapy, clear progression of disease was noted, with development of new pulmonary nodules and an increase in the size of the right-middle–lobe tumor. Since the addition of bevacizumab did not provide better tumor control, further treatment was switched to the chemotherapy doublet of carboplatin and paclitaxel, which induced a durable partial response. During her therapy with erlotinib, the patient experienced a mild rash on her face, chest, and back, which was treated with emollients and topical clindamycin. She had mild paronychia, which improved after topical therapy. The patient experienced alopecia after brain radiotherapy, and it persisted with very slow hair regrowth while she was receiving erlotinib. She had growth of dark, thick, coarse hairs on the dorsal aspect of her fingers as well. Three weeks after starting erlotinib, the patient noticed an accelerated growth of her eyelashes, which interfered with her wearing glasses because the lashes pushed against the lenses. She had to trim her eyelashes with scissors on a weekly basis. Close examination revealed marked bilateral coarse, thick, elongated irregular growth of the eyelashes with marked darkening and curling of the terminal ends (Fig 2). These changes resolved after erlotinib was discontinued when disease progressed.

Hypertrichosis of the eyelashes, or eyelash trichomegaly, was originally described in the setting of rare congenital conditions such as Oliver-McFarlane syndrome,4 oculocutaneous albinism type I,5 or familial hypertrichosis.6 Although it may be encountered in the context of generalized acquired hypertrichosis,7 hypertrichosis of the eyelashes is more often an isolated finding. It is defined as an increase in the length, thickness, stiffness, curling, and pigmentation of existing eyelashes.8 Acquired trichomegaly of the eyelashes has been repeatedly described in case series of patients infected with HIV type 19 or in association with uveitis.10 Trichomegaly has been reported in some patients secondary to therapy with a drug such as the antiretroviral agent zidovudine (a reverse transcriptase inhibitor),11 and is usually associated with poor tolerance to the drug. Topical ocular hypotensive (antiglaucoma) agents such as latanoprost12 and bimatoprost13 have on rare occasions caused trichomegaly of the eyelashes. Other ocular topical treatments such as cyclopentolate14 and systemic therapy with the anticonvulsant topiramate8 also have been reported to cause trichomegaly. The condition was noted in some recipients of solid organ transplants who were given cyclosporine15 or tacrolimus.16 Acquired trichomegaly was reported in isolated cases of patients with dermatomyositis17 and systemic lupus erythematosus18 (Table 1). In cancer patients, trichomegaly must be distinguished from a rare paraneoplastic syndrome, the acquired hypertrichosis lanuginosa, characterized in adults by the abnormal growth of lanugo-type hair, confined to the face and neck and concomitant with the spread of an internal malignancy.19,20 Trichomegaly can occur in patients with cancer in the setting of a paraneoplastic syndrome,21 or secondary to anticancer...

Trichomegaly of the Eyelashes After Lung Cancer Treatment with the Epidermal Growth Factor Receptor Inhibitor Erlotinib

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therapy with interferon-α.22 With the introduction of EGFR inhibitors in clinical practice, clinicians have observed numerous cutaneous adverse effects, such as acneiform rash, pruritus, and, less frequently, xerosis, paronychia, skin fissures, and telangiectasia.23 After treatment with the recombinant anti-EGFR antibody cetuximab, generalized diffuse trichomegaly can occur.24 Eyelash trichomegaly has been encountered after treatment with cetuximab as well25 and after the EGFR tyrosine kinase inhibitors erlotinib26,27 and gefitinib.28,29 In these cases, trichomegaly occurred after about 2 months of therapy and was reversible after cessation of the medication. Because of the risk of trichiasis and secondary corneal ulceration,27 it has been recommended that patients with trichomegaly who complain of symptoms of eye irritation be seen by an ophthalmologist, because other ocular conditions such as conjunctivitis and keratoconjunctivitis sicca can complicate anti-EGFR therapy. Trimming and epilation have been found to be satisfactory, safe therapeutic options. As illustrated in our case report, sensitivity to EGFR tyrosine kinase inhibitors in non–small-cell lung adenocarcinomas has been associated with somatic mutations in the EGFR gene1-3 with subsequent constitutive ligand-independent activation of the receptor kinase and prolonged kinase activity after ligand stimulation.2,30 EGFR tyrosine kinase domain mutations are mainly either in-frame deletions in exon 19, a single-point missense mutation in exon 21, or in-frame duplications, insertions, or both in exon 20.31 Retrospective data showed average response rates to EGFR tyrosine kinase inhibitors of approximately 75% for tumors with EGFR mutations, and, in contrast, less than 10% for tumors with the wild-type EGFR gene.32 The patient presented here had a deletion mutation in exon 19, and exhibited an excellent long-lasting response to erlotinib. The exact incidence of eyelash trichomegaly is unknown, and the condition remains sporadically reported. Although it appears to be a class effect associated with EGFR inhibitors, the occurrence of eyelash trichomegaly in relation to EGFR mutations is unknown. Whether eyelash trichomegaly correlates with

![Fig 1.](image1)

![Fig 2.](image2)
clinical response of lung cancer to EGFR inhibitors or whether it occurs as an unrelated adverse event remains to be evaluated on a larger scale. We are planning to investigate further the effect of erlotinib on the eyelashes of patients with lung cancer who receive erlotinib for adjuvant therapy or for secondary prevention.

Fadi Braiteh and Razelle Kurzrock

Department of Investigational Cancer Therapeutics, Phase I Program, The University of Texas M.D. Anderson Cancer Center; and The University of Texas Graduate School of Biomedical Sciences Houston, Houston, TX

Faye M. Johnson

Department of Thoracic/Head and Neck Medical Oncology, The University of Texas M.D. Anderson Cancer Center; and The University of Texas Graduate School of Biomedical Sciences Houston, Houston, TX

AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

REFERENCES


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